CLAIM LISTING

1-8 Cancelled

9 (Newly presented) In a bioassay for the detection in human bodily fluids of a target carbohydrate antigen that is characteristic of a bacterium causative of human ear and respiratory tract infections, which bacterium also is known to colonize the nasopharyngeal area of children of an age up to about 12 years without causing infection, the improvement which reduces the incidence of results falsely indicative of the presence of infection in said children who are nasopharyngeally colonized but are otherwise healthy, which improvement maintains the sensitivity of said bioassay to the presence in bodily fluids of said carbohydrate antigen and also maintains the specificity of said bioassay at not less than 90%, and consists in reducing the total amount of antibodies to said carbohydrate antigen employed per test by an amount that is determined empirically in identical bioassay tests in which the amount of antibody present is varied and bioassay tests are run identically for each variation on samples of bodily fluid taken from both (1) otherwise healthy children known to be nasopharyngeally colonized by the bacterium of which the antigen is characteristic and (2) children known to have an ear or respiratory infection caused by the same bacterium.

10 (Newly presented) A bioassay according to Claim 9 wherein the target antigen is a carbohydrate antigen characteristic of a bacterium selected from among *Streptococcus pneumoniae*, nontypable *Haemophilus influenzae, Moraxella catarrhalis* and *Staphylococcus aureus*.

11 (Newly presented) A bioassay according to Claim 9 wherein the target antigen is the C-polysaccharide cell wall antigen common to all serotypes of *Streptococcus pneumoniae*.

12 (Newly presented) A bioassay according to Claim 11 conducted on an immunochromatographic ("ICT") test strip upon which (a) tagged antibodies to the target carbohydrate antigen have been movably deposited near the sample introduction end of said strip, whereby liquid sample, upon introduction to the strip, picks up the movable deposit of said tagged antibodies and flows together therewith along the strip, thereby enabling formation of tagged antibody-antigen conjugates if target antigen is present in the sample, and (b) antibodies to the target antigen have been immovably deposited to form the capture line located near the end of said strip remote from its sample introduction end, so that tagged antibody-antigen conjugates in the flow stream of sample and tagged antibody react with said immovable antibodies to form tagged antibody-antigen-immovable antibody "sandwiches" upon contact, causing tag to mass upon the capture line.

13 (Newly presented) A bioassay according to Claim 12 wherein the antibodies are antibodies to the C-polysaccharide antigen of *Streptococcus pneumoniae* which have been affinity purified, the tag material is colloidal gold and the total amount of antibodies needed per bioassay to reduce the incidence of results falsely indicative of the presence of infection in children who are nasopharyngeally colonized with *Streptococcus pneumoniae* but otherwise healthy has been determined in empirical tests, and is attained by (a) placing the movable deposit of tagged antibodies on the ICT strip by applying a solution of said antibodies having an optical density of 1.5 and (b)

depositing the immovable antibodies constituting the capture line from a solution containing 0.3 mg./ml.of antibodies delivered to the strip at a rate of 0.5 ml. per 6 mm. of strip with the delivery tip of a precision pump.

14 (Newly presented) In an ICT bioassay for the detection in human bodily fluids of a carbohydrate antigen that is characteristic of a bacterium causative of human ear and respiratory tract infections, which bacterium also frequently colonizes the nasopharyngeal area of children of an age up to about 12 years without causing infection, the improvement which reduces the incidence of test results falsely indicative of the presence of infection in said children who are nasopharynegeally colonized but are otherwise healthy, which improvement maintains the sensitivity of said bioassay to the presence in said bodily fluids of said carbohydrate antigen and also maintains the specificity of said bioassay at not less than 90% and consists in adding at least one immovable "scrub" line on the test strip, located just prior to the capture line in the sample flow path of the ICT test strip, for the purpose of removing excess target antigen in the sample by "scrubbing out" an identical portion of said target antigen from samples of bodily fluid obtained from both (a) otherwise healthy children who are nasopharygeally colonized by the bacterium of which the target antigen is characteristic and (b) children who are infected by the same bacterium, wherein the number of capture lines, the concentration of antibody deposited on each capture line and the extent, if any, to which the concentration of antibodies otherwise employed in the test is modified in order to obtain the stated results have all been determined empirically in bioassay tests wherein each of (i) the number of "scrub" lines, (ii) the concentration of

antibody on each "scrub" line, and (iii) the total amount of antibodies otherwise present, per test, were determined in identical bioassays representing each variation that were run identically on samples of bodily fluid taken from each of (1) otherwise healthy children known to be nasopharyngeally colonized by the bacterium of which the target antigen is characteristic and (2) children known to have an ear or respiratory infection caused by said bacterium.

II. STATUS OF COPENDING APPLICATIONS

Applicants regret that this application as filed contains an inadvertent but pervasive typographical error whereby it refers to the commonly owned, copending U.S. patent application Serial No. 09/397,110 as " 09/399,710" in multiple places. It is noted that this application does *not correspond to Patent No. 6,409,683* which, as the Action correctly observes "has nothing in common with the instant application or invention."

Applicants note that the correct application number, Serial No. 09/397,110, does appear in the present application in the final line of original page 6.

New specification pages 2, 4, 5, 7, 8 and 11 are supplied herewith, in Appendix A, to correct this error. New page 4 expressly incorporates Application Serial No. 397,110 herein by reference. Application Serial No. 397,110 has been allowed, its final fee has been paid and it should therefore issue soon.

Applicants sincerely apologize to the Examiner for the inadvertent, pervasive typographical error and the difficulties thereby unintentionally created in connection with the examination of this application.

III. RESPONSE TO REJECTION UNDER 35 U.S.C. §112, 1ST PARAGRAPH

Applicants have *not* incorporated herein by reference commonly assigned, copending U.S. patent application Serial No. 09/518,165 but are relying upon it only as a prior filed, copending application containing additional pertinent information.

Applicants submit that the present application which clearly referred as filed to Application Serial No. 09/397,110 at p.6, last line and, in its last paragraph, p.10, pointed to the fact that all the examples herein employ antibodies to *Streptococcus pneumoniae* treated as therein described in detail, to render them specific to the C-polysaccharide cell wall antigen present in all serogroups of *S. pneumoniàe*, contains a wholly enabling disclosure which complies fully with 35 U.S.C. §112. Moreover, since the correct application *was* referred to at least once in the application as filed, a person of ordinary skill in the art, recognizing "09/399,710" to be an incorrect number even as the Examiner has done, would have consulted Application Serial No. 09/397,110 and almost instantly have recognized it to be the copending, commonly assigned application intended to be referred to throughout and have understood that its disclosure of how to obtain purified antigen-specific antibodies capable of recognizing the C-polysaccharide antigen of *S. pneumoniae* with exceptional specificity and sensitivity is all that is needed to complete the explanation herein of exactly how to achieve the results specifically disclosed herein, in connection with modifying a bioassay for *S. pneumoniae* to reduce the incidence of false positive tests for infection obtained on samples of bodily fluid (such as urine) obtained from nasopharyngeally colonized but otherwise healthy children under the age of about 12.

IV. REJECTIONS UNDER 35 U.S.C. §112 SECOND PARAGRAPH

By this amendment, the previously submitted claims have been cancelled and new claims are presented. In drafting them, an earnest effort has been made to avoid the expressions that the action specifically objected to and/or held to be indefinite and confusing or vague.

In the examples of this application, modifications to the Binax, Inc. commercially available, NOW® assay for *S. pneumoniae*, which is described and claimed in Application Serial No. 09/397,110 and is the only such assay the FDA has to date approved for detection of *S. pneumoniae* in human patient samples were made by, experimentally varying it (i) as to total antibody content, (ii) to reduce antigen content in the sample by "scrubbing" out a portion thereof with one or more pre-capture line "scrub" lines and (iii) in combinations of (i) and (ii). In each instance, samples of urine from *each* of (i) healthy but nasopharyngeally *S. pneumoniae*-colonized children and (ii) children having *S. pneumoniae*-caused ear or respiratory infections, were identically tested and an overall evaluation of the test results was made. The experimental variations of the tests were selected empirically. In evaluating the test results and deciding how best to modify the NOW ® test to accomplish a significant diminution in test results falsely indicative of the presence of *S. pneumoniae*-induced disease obtained on samples from otherwise healthy but nasopharyngeally colonized children, it was necessary to maintain the established sensitivity of the test and to keep its specificity at a figure of at least 90%. It was determined from evaluation of the experimental test results that the combination of (1) using a solution of gold-tagged antibodies (affinity purified before tagging as described

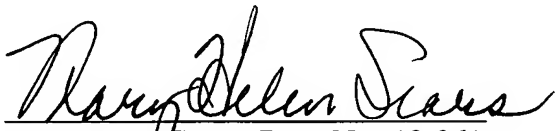
in Serial No. 09/397,110) having an optical density of 1.5 to place a movable deposit of tagged antibodies on the ICT strip near the point of sample introduction and (2) applying the stripe of immovable antibodies that make up the capture line from a solution of 0.3 mg./ml. delivered at the rate of 0.5 ml. per 6 mm. of ICT strip width from the delivery tip of a precision pump best achieved the criteria of sensitivity, specificity and diminution of false disease-indicative results obtained on fluid samples obtained from healthy but colonized children.

This modification of the test is critical to assist in ensuring that otherwise healthy children in the age group in which nasopharyngeal colonization frequently occurs are not mistaken for diseased children and given medication that is unneeded and may even be detrimental to their health and well being. It is noted, in particular, that both the Dowell abstract cited at p.4 of the action and the Adegbola *et al* article quoted on the same page describe test results obtained with the NOW ® test *prior* to the undertaking of the work disclosed in this present application. This application, combined with the disclosure of Appln. Serial No. 09/397,110 concerning all the steps needed to achieve satisfactory antibody affinity purification, clearly teaches how the problem of false positive test results obtained in otherwise healthy, but nasphoaryngeally- *S. pneumoniae*-colonized children was solved. In this regard, it is emphasized that, while the Examiner has correctly appreciated that the result disclosed and claimed could not have been achieved with a randomly selected batch of *unpurified* antibodies raised against *S. pneumoniae*, this result has been achieved with antibodies treated in precisely the same way as those used in the commercial NOW ® *S. pneumoniae* test prior to its modification, as herein disclosed and claimed, to reduce the total amount of antibodies present per test.

V. CONCLUSION

It is believed that this amendment places this application in condition for allowance. Should the Examiner believe that further adjustments and changes in the claims are needed, Applicants' counsel invites arrangement of a telephone or personal interview, as preferred, via a telephone call to such counsel at the number set forth below.

Respectfully submitted,



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